COMMENTARY

Psychodermatology in the Era of COVID-19

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J Clin Aesthet Dermatol. 2021;3(3 Suppl 1):S24–S27

ABSTRACT

The impact of the coronavirus disease 2019 (COVID-19) pandemic on mental health has been reflected in different populations worldwide. It has caused significant psychopathological consequences in general population, healthcare professionals (e.g., dermatologists), patients with COVID-19, and patients with other diagnoses, including skin diseases. The prevalence of psychiatric comorbidities in dermatology has long been reported to be at least 30 percent. It is important to investigate the pandemic's impact on comorbid psychosocial and psychopathological symptoms seen in dermatology, including expected short- and long-term mental health consequences. The authors seek to raise awareness among healthcare professionals of the impact that COVID-19 is having on existing psychodermatological conditions and discuss the practical implications of this relationship in dermatology.

KEYWORDS: COVID-19, dermatology, mental disorders, mental health, psychodermatology, pandemics, skin diseases, stress, psychological

The coronavirus disease 2019 (COVID-19), has placed a significant psychosocial burden on different patient populations in various medical settings.[1] Despite these widespread effects, few studies have been published exploring the impact of COVID-19 on psychiatric symptomatology (e.g., anxiety, depression) commonly seen in patients with certain skin disorders (e.g., atopic dermatitis, psoriasis). Before the pandemic, the prevalence of psychiatric comorbidities in patients with dermatological diagnoses was reported to be at least 30 percent,[2] but the mid- and long-term impact of the pandemic on psychiatric symptoms associated with skin disorders has not yet been estimated or clearly defined.

This new era has ushered in unprecedented challenges in mental health. Feelings of hopelessness and frustration regarding safety concerns, the previous lack of definitive treatment for COVID-19, and socioeconomic impact of the pandemic (e.g., quarantining, isolation, financial hardships from loss of jobs and businesses) have led to significant emotional distress in many individuals and an upsurge in several mental disorders, creating complex psychosocial dynamics.[3–5] At the same time, these challenges are shared by the world as a whole, which has led to increased feelings of empathy for the suffering of others on a global level among all people with vested interest in the functioning of society.[4] The impact of this pandemic on mental health has been reflected in different populations, with significant psychological consequences in the general population, healthcare professionals (e.g., dermatologists), patients with COVID-19, and patients with other diagnoses.[1,6] In a review exploring the epidemiology of psychiatric illness related to the COVID-19 pandemic, Hossain et al[1] reported an increased prevalence in anxiety disorders, depression, posttraumatic stress disorder (PTSD) symptoms, sleep disorders, somatic symptoms, and suicidal behavior, which are similar to those observed in populations following natural disasters.[1] Brooks et al[5] conducted a review on people with severe acute respiratory syndrome (SARS), Ebola, H1N1 influenza, Middle East respiratory syndrome, or equine influenza and reported long-lasting psychological effects related to quarantining.[5] This underscores the need for dermatologists to closely monitor their patients with dermatologic diagnoses associated with mental health issues, such as depression and anxiety. In other words, the known pathophysiological connection between the skin and the brain, along with the notable social changes occurring as a result of the COVID-19 pandemic, might logically predict a higher incidence of comorbid psychopathology in patients suffering from psychodermatological disorders.

Psychodermatologic disorders can be broadly classified into the following four groups

1. Psychophysiological dermatoses. This group includes skin diseases triggered or worsened by psychological stress, such as psoriasis or chronic spontaneous urticaria.

FUNDING: No funding was provided for the preparation of this article.
DISCLOSURES: The authors have no conflicts of interest relevant to the content of this article.
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2. **Primary psychopathology focused on the skin.** This group includes skin disorders for which there is no primary dermatosis, but there are skin symptoms or self-inflicted skin lesions that are manifestations of an underlying psychiatric illness and/or a psychological dynamic (e.g., delusional infestation, skin picking and factitious disorders).
3. **Cutaneous sensory disorders.** This group includes unpleasant skin sensations that may or may not elicit the desire to scratch, including not only itching, but also dysesthesia, involving symptoms such as stinging, tingling, burning, allodynia, or numbness. These patients do not present with a primary dermatosis and they may or may not present with secondary dermatologic lesions. This group of disorders may be linked with a neuropathic mechanism, where stress may play a relevant role, and/or psychosocial aspects that are less clearly defined.
4. **Dermatoses leading to psychosocial comorbidities.** This group includes disfiguring skin conditions that contribute to psychosocial distress, such as psoriasis or alopecia areata.[7]

When considering the higher prevalence of psychiatric symptoms among the above-described patient populations, along with the current increase in mental disorders among the general population due to the pandemic, it stands to reason that patients with psychodermatological disorders, such as psoriasis, alopecia areata, or chronic urticaria, would be at greater risk of psychiatric illness and comorbid skin disease (onset or relapse), than before the pandemic.

Kutlu et al[8] reported an increase of diagnoses of alopecia areata two months after the novel coronavirus outbreak, suggesting a link between stressors related to COVID-19 (e.g., unemployment, deaths) and the disease. This is corroborated by previous studies documenting a statistically significant association between alopecia areata and stressful life events in the previous six months.

Shen et al[9] observed that income loss due to the pandemic correlated with an increase in disease activity in patients with chronic urticaria, with perceived stress assessed by a visual analogue scale.[9]

A web-based survey performed by Kuang et al[10] reported an association between income loss and outdoor activity restriction and exacerbation of psoriasis, perceived stress, and symptoms of anxiety and depression. This study also observed higher prevalence of nonadherence to treatment independently associated with patient-reported outcomes of psoriasis, a finding that was also linked with pandemic-related stress, income loss, and quarantine.[10]

A cross-sectional study conducted by Guo et al,[11] which assessed the link between COVID-19-related effects (e.g., income loss, outdoor activity restriction, unemployment) and health outcomes (e.g., anxiety, depression, perceived stress) in Chinese patients with several skin diseases, demonstrated the relative immediate effects of this pandemic on quality of life impairment and mental illness.[11] Among the skin diseases included in the study, some were in the groups "psychophysiological dermatoses" and "dermatoses leading to psychosocial comorbidities," namely allergic skin diseases, papulosquamous disorders, hair disorders, and pigmentary diseases. This study reinforced the impact of social changes related to the pandemic and the expected higher mental health impairment in a vulnerable population where a previous psychopathological comorbidity is common.

These findings may be even more relevant in patients with existing psychodermatological disorders who are also COVID-19 survivors. In a study of COVID-19 survivors, Mazza et al[12] reported a higher prevalence of anxiety disorders, depression, PTSD symptoms, sleep disorders (e.g., insomnia), and obsessive-compulsive disorder (OCD) symptoms. As might be expected, the authors observed increased scores in patients who also presented previous psychopathology.[12]

Recent studies have argued that the medium- and long-term psychopathological effects of COVID-19 among survivors of the virus may not solely be a consequence of the social changes linked with the pandemic. The effects may also be a result of the systemic inflammation triggered by the infection, which involves immune-inflammatory pathways that have been well described in the etiopathogenesis of psychiatric disorders, as well as a possible result of neuroinvasion of the virus.[13]

COVID-19 patients have been noted to present with increased levels of inflammatory markers, including Interferon-γ, Interleukin (IL)-1β, and IL-6. Immune dysregulation involving these inflammatory markers is also a core feature in depression and PTSD.[12–14] In the prospective cohort study by Mazza et al,[12] which evaluated the psychopathological impact of COVID-19 in survivors at a one-month follow-up visit, baseline inflammatory markers measured in the acute phase response (neutrophil/lymphocyte ratio, monocyte/lymphocyte ratio, and systemic immune-inflammation index [i.e., platelet count x neutrophil count / lymphocyte count]) were associated with the later development of OCD symptoms. This is consistent with Banerjee's findings, which suggested that the immune-inflammatory dysfunction caused by the virus, along with heightened perception of risk of contamination, resulted in excessive hoarding (e.g., masks and disinfectants) and hand-washing in individuals with pre-existing OCD and/or hoarding disorders.[15]

These findings are relevant in psychodermatology, particularly concerning self-inflicted skin lesions. Although some patients may also exhibit impulsive features, skin picking disorders are typically related to symptoms of OCD.[5] Furthermore, patients with skin picking disorders frequently exhibit a higher prevalence of other psychiatric comorbidities, namely anxiety, depression, and PTSD, prevalence of which have all increased since the start of the COVID-19 pandemic.[16] Additionally, the boundary between obsession and delusion is not rigid—an obsession can coexist or even evolve into a delusion, which can also be observed in patients with a pre-existing diagnosis of a skin picking disorder.[7] Perceived risk of contamination seems to play a role in the increasing incidence of OCD symptoms observed during this pandemic.[12,15] In turn, an increasing incidence of psychotic disorders, where contamination is a frequent delusion content, has also been documented in relation to the COVID-19 pandemic, with a multifactorial etiology in vulnerable patients, including viral exposure, psychological stress, significant social changes, and the role of neuroinflammation, with up-regulation of IL-6 and IL-1β.[17] This suggests the need to pay more attention to delusional infestation in psychodermatology.

Considering the biological features of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), neurotropism may be also a key feature in understanding the etiopathogenesis of psychiatric comorbidities. SARS-CoV-2 can enter the cell through the plasmalemmal angiotensin-converting enzyme 2 (ACE2), and there is an important expression of ACE2 in other tissues, including the endothelium, the neurons, and neuroglia. The routes of neuroinvasion could involve the hematogenous pathway with the following mechanisms:

- SARS-CoV-2 binding to the ACE2 receptors in the endothelium and then inducing a dysfunction of the blood brain barrier (BBB)
- Passing this BBB in the setting of increased permeability due to the systemic inflammation
- Directly passing into the central nervous system (CNS) through structures with little protection of the BBB, such as the circumventricular organs.
- Using immune peripheral cells to access the CNS.

A neuronal pathway, such as the olfactory pathway, involving peripheral nerves has also been suggested.[17,18] Once in the CNS, peripheral inflammatory mediators and inflammatory cells may lead to a neuroinflammation, which can be exacerbated by the chronic stimulation of the hypothalamic-pituitary-adrenal (HPA) axis through the physical and psychological stress caused by COVID-19 infection. This is also relevant in the etiopathogenesis of psychiatric illness, such as depression.[18] Furthermore, depression is a significant psychiatric comorbidity in psychodermatological dermatoses. Globally, the etiological link between depression and those dermatoses is bidirectional, involving dysfunction of the central HPA axis and interplay with the peripheral HPA axis in the skin. The effector cells include mast cells, the hair follicle, and epidermal keratinocytes, which secrete corticotropin-releasing hormone (CRH) and express its receptor. Keratinocytes express IL-18, and mast cells activate pro-IL-18 into IL-18. IL-18 modulates mast cells and plays a central role in cutaneous inflammatory diseases.[19–21] Thus, a higher incidence of psychopathology in patients with those dermatoses and COVID-19 (patients and/or survivors) could be expected. These physiopathological mechanisms could also justify the onset or worsening of psychodermatological dermatoses in patients with COVID-19.[8]

Regarding the connection among HPA axis dysfunction, psychiatric illness, and psychodermatology, it is relevant to investigate a link between psychodermatological disorders and PTSD. In PTSD, defective glucocorticoid signaling and pro-inflammatory state are observed, sharing physiopathological mechanisms with psychodermatological dermatoses, namely psoriasis.[14] In addition, chronic urticaria may occur in relation to the delayed-onset subtype of PTSD, a finding that may shed light on possible psychosomatic consequences of this pandemic.[22] Moreover, we may suppose that a higher incidence of other psychodermatological disorders, particularly those belonging to the group "cutaneous sensory disorders," could also be expected as medium- or long-term effects of the pandemic. Psychogenic pruritus (a type of chronic pruritus that is not associated with a primary dermatosis or systemic disorder and where psychosocial factors and psychopathology are related to the symptoms, possibly with a deep connection with dissociative mechanisms) is one such disorder.[7] Dissociation is associated with PTSD, anxiety disorders, and depression, which represent the burden of psychiatric illness linked with this pandemic.[23] This topic deserves prospective studies in psychodermatology, namely cutaneous sensory disorders and self-inflicted skin lesions, including both skin-picking and factitious disorders.

Finally, an in-depth understanding of psychopathology related to the pandemic and its impact on psychodermatology should include "Attachment Theory," developed by John Bowlby.[24] The COVID-19 outbreak has been associated with signs of insecure attachment in children, exacerbated by factors that limit the contact with family and peers and increased levels of anxiety and depression, which are two paradigmatic examples of psychiatric illness linked with the human response to a threat. Since the relevance of attachment continues throughout life, the social changes imposed by the pandemic challenge an important social characteristic of humans, from childhood to adulthood: interpersonal relationships, both by separation from attachment figures and the fear to be in contact with other people.[25] Therefore, dysfunctional attachment is correlated with a physiopathological response to psychosocial stress and psychopathology, with relevance in psychodermatology, particularly in the era of COVID-19.

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